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**DATE:** December 19, 2005

**PTO IDENTIFIER:** Application Number 08/728,463-Conf. #2701  
ALLOWED SEPTEMBER 20, 2005  
ISSUE FEE DUE DECEMBER 20, 2005\*\*\*

**Inventor:** Nils Lonberg et al.

**MESSAGE TO:** US Patent and Trademark Office  
Examiner P. J. Nolan  
**C/O SUPERVISOR:** CHRISTINA CHAN  
Art Unit 1644  
**FAX NUMBER:** (571) 273-8300

**FROM:** DARBY & DARBY P.C.

Jeffrey C. Pepe

**PHONE:** (206) 262-8911

**Attorney Dkt. #:** 04280/1201643-US2

**PAGES (including Cover Sheet):** 24

**CONTENTS:** COPY of Auto-Reply Fax Transmission (1 page)  
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Copy of IDS Postcard (1 page)  
Copy of IDS of 01/24/97 (2 pages)  
Copy of PTO-1449 (12 pages)  
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Dear Ms. Chan - Further to my voice mail message of today, we ask that this IDS be signed off and returned via facsimile by Tuesday, 12/20/05 so that we may pay the issue fee in this application. Your help in this matter is greatly appreciated.

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<b>FAX TRANSMISSION</b>			
<b>DATE:</b> October 28, 2005 <b>PTO IDENTIFIER:</b> Application Number 09/718,463-Conf. #2701 <b>Inventor:</b> Nils Lohberg et al. <hr/> <b>MESSAGE TO:</b> US Patent and Trademark Office Examiner P. J. Nolan Art Unit 1644 <b>FAX NUMBER:</b> (571) 273-8300 <hr/> <b>FROM:</b> DARBY & DARBY P.C. Jeffrey C. Pepe <b>PHONE:</b> (206) 262-5911 <b>Attorney Dkt. #:</b> 042801201643-L52 <hr/> <b>PAGES (Including Cover Sheet):</b> 22 <b>CONTENTS:</b> <ul style="list-style-type: none"> <li>Certificate of Transmission (1 page)</li> <li>Transmittal (1 page)</li> <li>Request For Acknowledgment Of Previously Submitted Information Disclosure Statement (IDS) (2 pages)</li> <li>Copy of IDS (Postcard (1 page)</li> <li>Copy of IDS of 09/24/92 (2 pages)</li> <li>Copy of PTO-1449 (12 pages)</li> <li>Copy of References Sent Postcard (1 page)</li> <li>Copy of Transmittal of References Sent on 03/09/01 (1 page)</li> </ul> <b>PLEASE DELIVER TO EXAMINER NOLAN AS SOON AS POSSIBLE</b>			
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PAGE 1/24 * RCVD AT 12/19/2005 5:08:56 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-6/33 * DNI:2738300 * CSID:2062628901 * DURATION (mm:ss):10-12			

# FAX TRANSMISSION

**DATE:** October 28, 2005

**PTO IDENTIFIER:** Application Number 08/728,463-Conf. #2701  
ALLOWED SEPTEMBER 20, 2005

**Inventor:** Nils Lonberg et al.

**MESSAGE TO:** US Patent and Trademark Office  
Examiner P. J. Nolan  
Art Unit 1644

**FAX NUMBER:** (571) 273-8300

**FROM:** DARBY & DARBY P.C.

Jeffrey C. Pepe

**PHONE:** (206) 262-8911

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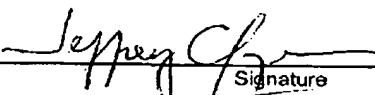
Application No. (if known): 08/728,463

Attorney Docket No.: 04280/1201643-US2

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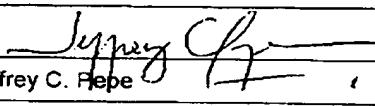
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<b>TRANSMITTAL FORM</b> <i>(to be used for all correspondence after initial filing)</i>		Application Number	08/728,463-Conf. #2701
		Filing Date	October 10, 1996
		First Named Inventor	Nils Lonberg
		Art Unit	1644
		Examiner Name	P. J. Nolan
Total Number of Pages in This Submission	22	Attorney Docket Number	04280/1201643-US2

ENCLOSURES (Check all that apply)		
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<input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	Request for Acknowledgement of IDS (2 pp), Copy IDS Postcard (1 page), Copy IDS of 1/24/97 (2 pages), Copy of PTO-1449 (12 pages), Copy of Refs Sent Postcard (1 page), Copy of Transmittal of Refs Sent (1 page), Certificate of Facsimile Transmittal (1 page), Fax Cover (1 page)	

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	DARBY & DARBY P.C.		
Signature			
Printed name	Jeffrey C. Repe		
Date	October 28, 2005	Reg. No.	46,985

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Docket No.: 04280/1201643-US2  
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:  
Nils Lonberg et al.

Allowed: September 20, 2005

Application No.: 08/728,463

Confirmation No.: 2701

Filed: October 10, 1996

Art Unit: 1644

For: TRANSGENIC NON-HUMAN ANIMALS  
FOR PRODUCING HETEROLOGOUS  
ANTIBODIES

Examiner: P. J. Nolan

**REQUEST FOR ACKNOWLEDGMENT OF PREVIOUSLY SUBMITTED  
INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Issue Fee  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Commissioner:

This application has been allowed and the issue fee is due December 20, 2005.

It has come to our attention that the Form PTO-1449 (12 pages) submitted with the initial Information Disclosure Statement (IDS) in the instant application, has not yet been acknowledged.

The IDS, Form PTO-1449, and 5 references were mailed on January 24, 1997 and received by the U.S. Patent and Trademark Office (USPTO) on January 28, 1997 (please see attached copy of return receipt postcard). The USPTO PAIR system shows that the IDS was filed, and a copy of the 2 pages of IDS appears on the Image File Wrapper on PAIR. However, a copy of the 12 pages of PTO-1449 does not appear on the Image File Wrapper for this application, nor do the 5 references submitted.

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Request For Acknowledgment Of Previously  
Submitted Information Disclosure Statement (IDS)  
Application No.: 08/728,463

2

Docket No.: 04280/1201643-US2

Our records also show that copies of these references were forwarded to Examiner Amy Decloux on March 9, 2001 and received by the USPTO on March 15, 2001 (see attached copy of Return Receipt Postcard and Transmittal form).

Accordingly, Applicants respectfully request that the 12 pages of PTO-1449, originally submitted January 28, 1997 (as noted above and enclosed herewith), be reviewed by the Examiner and acknowledged.

Applicants appreciate the Examiner's prompt response to this submission.

Dated: October 28, 2005

Respectfully submitted,

By   
Jeffrey C. Repe  
Registration No.: 46,985

DARBY & DARBY P.C.  
P.O. Box 5257  
New York, New York 10150-5257  
(206) 262-8900  
(212) 527-7701 (Fax)  
Attorneys/Agents For Applicant

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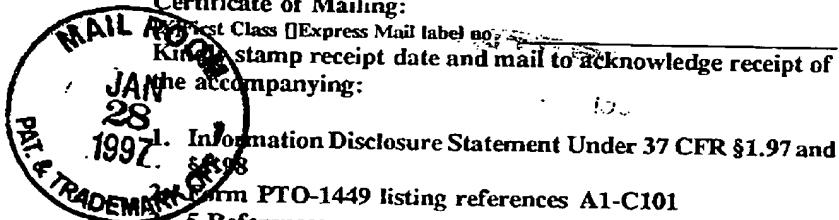
## APPLICANT: L.I.S LONBERG et al.

Title: TRANSGENIC NON-HUMAN ANIMALS FOR  
PRODUCING HETEROLOGOUS ANTIBODIES

Serial No: 08/728,463 Filed: October 10, 1995

Fee (if any) \$0.00 CheckEnclosed[] Yes[X] No

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1/24/97

TOWNSEND and TOWNSEND and CREW LLP

By Karen M. Williamson

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**PATENT**

Attorney Docket No. 014643-009020US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: )  
NILS LONBERG et al. ) Examiner: UNASSIGNED  
Application No.: 08/728,463 ) Art Unit: UNASSIGNED  
Filed: 10 October, 1996 ) INFORMATION DISCLOSURE  
For: TRANSGENIC NON-HUMAN ) STATEMENT UNDER  
ANIMALS FOR PRODUCING ) 37 CFR §1.97 and §1.98  
HETEROLOGOUS ANTIBODIES )  
)

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The disclosures cited on attached form PTO-1449 are being called to the attention of the Examiner. Copies of some of the disclosures (references A1-C96) are not being provided pursuant to 37 C.F.R. 1.98(d), as those disclosures have been previously cited by or submitted to the Patent Office in prior applications Serial Nos. 07/810,279, 07/853,408, 08/161,739, 08/165,699, 08/096,762, 08/352,322, and 08/209,741, to which the above identified application claims priority.

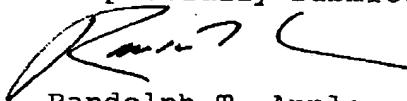
This information disclosure statement is being filed before the mailing date of the first office action on the merits.

Niels LONGBERG et al.  
Application No.: 08/728,463  
Page 2

PATENT

It is respectfully requested that the cited information be expressly considered during the prosecution of this application, and the disclosures be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Respectfully submitted,



Randolph T. Apple  
Reg. No. 36,429

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8th Floor  
San Francisco, California 94111-3834  
(415) 576-0200  
Fax (415) 576-0300  
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Mailing Date: March 9, 2001 First Class Mail  
File No.: 014643-009020us Attorney: ATS/ksj  
Application No.: 08/728,463 Filed: October 10, 1996 MAR 29 2001  
Inventor(s): LONBERGet al.  
Title: TRANSGENIC NON-HUMAN ANIMALS FOR PRODUCING  
HETEROLOGOUS ANTIBODIES

References cited in the Information Disclosure Statement previously filed and referenced in the parent case, application no. 08/352,322

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**3**

	<b>Application Number</b>	08/728,463
	<b>Filing Date</b>	October 10, 1996
	<b>First Named Inventor</b>	Lonberg, Nils, et. al.
	<b>Group Art Unit</b>	1644
	<b>Examiner Name</b>	DeCloux, Amy

Attorney Docket Number

14643009020

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Firm and Individual name	Townsend and Townsend and Crew LLP Andrew T. Serafini	Reg No. 41,303
Signature		
Date	03 09 01	

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*Mary Bernstein*

Signature

*Mary Bernstein*

Date

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v

FORM PTO-1449 (Modified)

LIST OF PATENTS AND PUBLICATIONS  
FOR APPLICANT'S INFORMATION  
DISCLOSURE STATEMENT  
(Use Several Sheets if Necessary)

PAGE 1 OF 12

Attorney Docket No.  
14643-009000Serial No.  
08/352,322Applicant  
NILS LONBERG and ROBERT M. KAYFiling Date  
December 7, 1994Group  
1804Reference DesignationU.S. PATENT DOCUMENTSExaminer

<u>Initial</u>	<u>Document No.</u>	<u>Date</u>	<u>Name</u>	<u>Class</u>	<u>Subcl:</u>	<u>File Date If Approp</u>
	A1 4,204,244	04/20/93	Fell et al.	435		
	A2 5,175,384	12/29/92	Krimpenfort	800		
	A3 5,434,340	07/18/95	Krimpenfort	800		

**COPY**FOREIGN PATENT DOCUMENTS

	<u>Document No.</u>	<u>Date</u>	<u>Country</u>	<u>Class</u>	<u>Subcl:</u>	<u>Trans. Yes No</u>
	B1 EP 0 315 062	05/10/89	EP			
	B2 WO 90/04036	04/19/90	PCT			
	B3 WO 90/12878	11/01/90	PCT			
	B4 WO 92/03918	03/19/92	PCT			
	B5 WO 91/10741	07/25/91	PCT			
	B6 WO 91/00906	01/24/91	PCT			

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

C1 Alt et al., Immunoglobulin genes in transgenic mice, TIG - August 1985

C2 Berman et. al., Content and organization of the human Ig V<sub>H</sub> locus: definition of three new V<sub>H</sub> families and linkage to the Ig C<sub>H</sub> locus, The EMBO J. 7:727-738 (1988)

C3 Berton et. al., Synthesis of germ-line γ1 immunoglobulin heavy-chain transcripts in resting B cells: Induction by interleukin 4 and inhibition by interferon γ, Proc. Natl. Acad. Sci. (U.S.A) 86:2829-2833 (1989)

C4 Bollag et al., Homologous recombination in mammalian cells, Annu. Rev. Genet. 23:199-225 (1989)

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PAGE 3 OF 11

Attorney Docket No. 14643-009000	Serial No. 08/352,322
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Applicant NILS LONBERG and ROBERT M. KAY
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Filing Date December 7, 1994
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Group 1804
---------------

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

- \_\_\_\_ C5 Bruggemann et al., Human antibody production in transgenic mice: expression from 100 kb of the human IgH locus, Eur. J. Immunol. 21:1323-1326 (1991)
- \_\_\_\_ C5(i) Bruggemann et al., A repertoire of monoclonal antibodies with human heavy chains from transgenic mice, Proc. Natl. Acad. Sci. USA 86:6709-6713 (1989)
- \_\_\_\_ C6 Bucchini et al., Rearrangement of a chicken immunoglobulin gene occurs in the lymphoid lineage of transgenic mice, Nature 326:409-411 (1987)
- \_\_\_\_ C7 Capecchi, The new mouse genetics: Altering the genome by gene targeting, TIG 5:70-76 (1989)
- \_\_\_\_ C8 Capecchi, Altering the genome by homologous recombination, Science 244:1288-1292 (1989)
- \_\_\_\_ C9 Coffman et. al., T cell activity that enhances polyclonal IgE production and its inhibition by interferon- $\gamma$ , J. Immunol. 136:949-954 (1986)
- \_\_\_\_ C10 Coffman et al., A mouse T cell product that preferentially enhances IgA production, J. Immunol. 139:3685-3690 (1987)
- \_\_\_\_ C11 Doetschman et al., Targetted correction of a mutant HPRT gene in mouse embryonic stem cells, Nature 330:576-578 (1987)
- \_\_\_\_ C12 Durdik et al., Isotype switching by a microinjected  $\mu$  immunoglobulin heavy chain gene in transgenic mice, Proc. Natl. Acad. Sci. USA 86:2346-2350 (1989)
- \_\_\_\_ C13 Esser and Radbruch, Rapid induction of transcription of unarranged Syl switch regions in activated murine B cells by interleukin 4, The EMBO J. 8:483-488 (1989)

EXAMINER

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PAGE 3 OF 11

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14643-009000Serial No.  
08/352,322Applicant  
NILS LONBERG and ROBERT M. KAYFiling Date  
December 7, 1994Group  
1804OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

C13(i) Ferrier et al., Separate elements control DJ and VDJ rearrangement in a transgenic recombination substrate, The EMBO J. 9:117-125 (1990)

C14 Forni, extensive splenic B cell activation in IgM-transgenic mice, Eur. J. Immunol. 20:983-989 (1990)

C15 Gerstein et al., Isotype switching of an immunoglobulin heavy chain transgene occurs by dna recombination between different chromosomes, Cell 63:537-548 (1990)

C16 Goodhardt et al., Rearrangement and expression of rabbit immunoglobulin κ light chain gene in transgenic mice, Proc. Natl. Acad. Sci. (U.S.A.) 84:4229-4233 (1987)

C17 Gordon, Transgenic mice in immunology, The Mount Sinai Journal of Medicine 53:223-231 (1986)

C18 Hagman et al., Inhibition of immunoglobulin gene rearrangement by the expression of a λ2 transgene, J. Exp. Med. 169:1911-1929 (1989)

C19 Ichihard et al., Organization of human immunoglobulin heavy chain diversity gene loci, The EMBO J. 7:4141-4150 (1988)

C20 Iglesias et al., Expression of immunoglobulin delta chain causes allelic exclusion in transgenic mice, Nature 330:482-484 (1987)

C21 James and Bell, Human monoclonal antibody production current status and future prospects, J. of Immunol. Methods 100:5-40 (1987)

C22 Jasin and Berg, Homologous integration in mammalian cells without target gene selection, Genes & Development 2:1353-1363 (1988)

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